

Expert Review of Neurotherapeutics

## **The effects of music listening interventions on cognition and mood post-stroke: A systematic review**

### **Abstract**

**Introduction:** Music listening may have beneficial psychological effects but there has been no comprehensive synthesis of the available data describing efficacy of music listening in stroke.

**Areas covered:** We performed a systematic review examining the effects of music listening interventions on cognition and mood post-stroke. We found five published trials (n=169 participants) and four ongoing trials. All studies demonstrated benefits of music listening on at least one measure of cognition or mood. Heterogeneity precluded meta-analysis and all included studies had potential risk of bias. Common reporting or methodological issues including lack of blinding, lack of detail on the intervention and safety reporting.

**Expert commentary:** It is too early to recommend music listening as routine treatment post-stroke, available studies have been under-powered and at risk of bias. Accepting these caveats, music listening may have beneficial effects on both mood and cognition and we await the results of ongoing controlled studies.

**Key words** (5-10 words): attention, cognitive impairment, depression, memory, mood, music, rehabilitation, stroke, systematic review

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## 1. Introduction

Stroke represents the second most common cause of death worldwide and is one of the commonest causes of adult disability. Globally the incidence and prevalence of stroke and related complications is increasing [1-3]. Psychological problems are common following stroke with one in four stroke survivors experiencing early post-stroke anxiety and depression [4], increasing to one in three at five years post-stroke [5]. A similar number are estimated to experience impairments in cognitive functioning post-stroke, particularly in the domains of attention, memory and executive function [6]. Cognitive deficits and mood disorders are known to be associated with poor functional recovery [7;8] and low quality of life following stroke [9]. Importantly, stroke survivors have rated psychological problems as the most important consequence of stroke, deeming this an important area further research [10].

Unfortunately, the evidence for interventions aimed at improving mood and reducing cognitive deficits post-stroke is sparse. We have evidence based drug treatments for stroke prevention but trials of pharmacological agents in mood and cognition have yielded disappointing results [11,12]. Non-pharmacological treatments have shown efficacy in other areas of mental health but have mostly failed to demonstrate suitable efficacy in stroke. For example, standard cognitive behavioural therapy (CBT), a psychological intervention recommended for mild to moderate depression in adults, lacks robust evidence in stroke survivors [12;13]. Although psychological interventions may have fewer side effects than pharmacological interventions, many of the currently available treatments require specialist skills, are costly, and potentially challenging to deliver in the presence of

stroke related cognitive impairments. Thus there is a pressing need for safe, efficacious and cost-effective treatments that are suitable for use following stroke [14].

There are plausible reasons to think that music based interventions may be one such safe and effective intervention. The beneficial effect of music in the treatment of mental disorders has been recognised for centuries [15]. Music has the ability to evoke emotions, affect arousal and to enhance performance on cognitive tasks. An underlying neural basis for the beneficial effects of music listening has been postulated [16]. Passively listening to music has been shown to promote changes in the limbic and paralimbic systems involving the amygdala, hippocampus, and nucleus accumbens [17]. Music is known to induce pleasure and influence changes in dopaminergic reward pathways in the brain [18;19;20]. Mood disturbances following stroke may have neuroanatomical and/or external aetiologies [21]. Alterations to neural transmission as a result of the brain injury may dysregulate reward pathways. Music interventions may act as an alternative means of priming the injured brain, inducing neural plasticity, and potentially reducing or remediating impairment [18]. For example, listening to preferred music has been shown to augment awareness of targets in the neglected area of space [22]. It has also been shown that listening to preferred music affects the default mode network, activating neural structures involved in autobiographical information, and episodic memory [23]. Recently, changes in grey matter volume in the frontal areas have been shown to be correlated with the recovery of verbal memory, focused attention, and language skills following music listening; in the same study changes in the limbic areas were correlated with reduced negative mood in individuals with stroke affecting the left side of the brain [24].

The use of music in medicine and in the treatment of neurological disorders is fairly new but evidence of utility is emerging. For example, music based interventions have been found to reduce depressive symptoms in adults [25], improve post-operative recovery [26], and reduce anxiety in individuals with dementia [27]. The way music based interventions are delivered varies greatly but fall into two broad categories: those delivered by certified music therapists and those delivered by non-specialists. Music therapists have specialist training and theoretical principles underpin their practice. Their specialist skills in the assessment and delivery of music interventions enable them to tailor the therapy to suit individual rehabilitation goals. Music listening based interventions on the other hand can be delivered by non-specialists making them less costly and resource intensive, albeit the effects of such interventions are less studied.

A systematic review assessing the usefulness of music therapy interventions following acquired brain injury (ABI) suggested that it may have beneficial effects on physical function by improving gait parameters [28]. Reports of potential effects of music listening on psychological outcomes post-stroke are available but there has been no comprehensive synthesis of the available data.

We aimed to determine the effects of music listening on psychological outcomes of cognition and mood in stroke survivors, by collating available data from controlled trials.

## **2. Methods**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) best practice guidance for design, conduct and reporting of this systematic review.

The review protocol was registered with PROSPERO, number CRD42015024416.

## ***2.1 Search strategy and selection criteria***

We used a concept based search strategy with search terms relating to stroke and music listening (see supplementary materials for details). Stroke terms were based on a validated search string from the Cochrane Stroke group; for music listening we used medical subject headings (MeSH) and other controlled vocabulary. We combined these two concepts with the Cochrane filter for controlled trials. We operated no language restrictions.

One of the review authors trained in systematic review (RS-P), conducted the primary database searches of 14 databases (supplementary materials) for identification of studies up to June 2015. Titles and abstracts generated from the electronic database searches were screened for relevance. Irrelevant titles and abstracts were excluded and full-text articles inspected to determine eligibility. As a test of internal validity, a second reviewer experienced in evidence synthesis (TQ) reviewed a random selection of 1000 titles from the search. As a test of external validity, this author (TQ) pre-selected two studies relevant to the study question and we assessed whether the search included these studies. Two independent reviewers (SB, GP) further assessed potentially relevant studies for inclusion. We resolved all disagreements by discussion, with the source data reviewed where needed. In addition to database searches, we hand searched conference proceedings, specialist music titles, trial registers and attempted to contact research teams we knew to be active in designing music interventions for neurological conditions (supplementary material). We operationalised studies of interest using the PICOS paradigm:

**Population:** Our population of interest comprised adult stroke survivors. We included studies using a “mixed” population (e.g. stroke and traumatic brain injury) if the proportion

of stroke survivors was greater than 70%. Where the proportion of stroke survivors could not be determined from the publication or through attempt to contact the study authors, the study was included. We included markers of case-mix, such as time since stroke, but no studies were excluded on the basis of these variables.

**Interventions:** We included any music listening component regardless of who provided the intervention, the primary purpose of the intervention, or the amount of intervention delivered. We excluded studies with a music playing focus or dance based therapy, where active music listening was not the primary focus. We also excluded studies with a solely rhythm based intervention (for example, metronome based speech or gait assistance) as well as studies using music listening as part of a complex (multi-modal) intervention unless the data allowed for quantification of the music based effect alone.

**Controls:** We accepted any other type of intervention (“active control”); treatment as usual, or no care as suitable controls.

**Outcomes:** Our primary interest was psychological outcome, with a focus on depression and cognition. We included any quantitative measure of cognition, mood, behaviour or associated clinical diagnosis. We included brief cognitive screening tests (for example, the Mini-Mental State Examination [MMSE]), detailed single and multi-domain neuropsychological assessments, and clinical diagnosis made using any recognised classification (for example, International Classification of Disease [ICD-10], Diagnostic and statistical manual of mental disorders [DSM-V]). We excluded studies with a surrogate outcome measure only (for example, functional brain imaging) and studies with only qualitative outcomes (n=3). Secondary outcomes of interest were related to user satisfaction and adverse outcomes.

**Study type:** We included controlled trials (randomised, quasi-randomised or non-randomised) but excluded case studies or case series with less than 10 participants.

## ***2.2 Data extraction and synthesis***

Data extraction (supplementary material) was performed by reviewers (SB, GP) working independently and using a study specific proforma, piloted on two relevant papers and refined where necessary.

## ***2.3 Meta-analysis, subgroup and sensitivity analyses***

We planned to pool data to give a summary of effect sizes using standard meta-analysis techniques, with subgroup analyses limited to "acute" (initial weeks) or "chronic" phase (those delivered later in the stroke journey) interventions. We also planned sensitivity analyses based on risk of bias.

## ***2.4 Risk of bias (quality) assessment of included studies***

We used the Cochrane Collaboration's Risk of Bias tool for randomised controlled trials (RCT) and the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS) to assess for risk of bias where appropriate. Both tools address key criteria such as selection bias, blinding, completeness of outcome data and selectivity of reporting. We modified the anchoring statements of the tool to suit our specific question.

## **3. Results**

Our test of internal validity found no papers on second review that were not identified on primary search. Our test of external validity found that our two pre-specified papers of interest [29,31] were included in initial title search.

We identified a total of 2073 titles from the initial search, of which 143 abstracts were assessed for inclusion following review of study titles. We reviewed 51 full-text articles and included five studies in the final review [29-33] with a total of 169 participants (90 [53%] male). We also found four unpublished studies of relevance and contacted authors to share data where possible (Figure 1). Characteristics of the included studies are summarised in Table 1 and results in Table 2.

There was substantial between-study clinical heterogeneity in the patients included, study design, interventions delivered and outcomes assessed. It would have been inappropriate to summarise data with meta-analyses and so we offer a narrative synthesis of the studies identified via systematic searches. Data did not allow for any of our pre-specified sensitivity or subgroup analyses.

**3.1 Population:** The number of participants included in each study varied from 14 to 60. The average age of participants was 60 years, and the average time since stroke varied from 8.7 days to 15 months. One of the studies did not state time since stroke [32]. All studies operated inclusion criteria to limit recruitment to specific stroke types. Three of the studies included individuals with unilateral neglect [29,30,33], one with middle cerebral artery stroke [31], and one with a mixed group of stroke and head injury patients [32].



**3.2 Intervention:** Choice of music could be made by patients or researchers. Two studies using researcher selected music used classical music (Bach, Vivaldi [30] and Mozart [33]) and one Hindustani ragas [32]. Participant selected music was from any genre of their choice. One study compared self-selected pleasant music to self-selected unpleasant music [29] and the other self-selected music to no music or audiobooks [31]. Method of intervention delivery was not reported for all studies but varied from using a music player with headphones or loudspeakers. Only one of the studies [31] reported using a music therapist to deliver the intervention in both in and outpatient setting. The duration of the listening intervention varied from a single testing session [30] to over three hours per day for six months [32].

**3.3 Outcomes:** Outcomes included mood and arousal, brief cognitive screen, detailed cognitive assessments, behavioural assessment of unilateral neglect and quality of life (Table 2). Some outcome assessments were carried out immediately before and after the listening intervention on the same day [29,30,33], others were carried out a few days before or several months after the music listening intervention [31, 32].

**3.4 Study design:** All three of the studies with a unilateral neglect group had a within-subject design with music listening compared to white noise, no music or verbal and tactile stimulation [29,30,33]. The two remaining studies were parallel-group randomised controlled trials (RCT) with music listening being compared to usual care [32], or usual care and another intervention (audiobook listening) [31]. None of the studies reported receiving financial support from commercial or industry partners. One of the studies was funded by national bodies and charities [31], one received no funding [29] and remainder did not disclose source of funding.

### 3.4.1 Mood and arousal

Mood and arousal were measured according to: a Visual Analogue Scale (VAS), heart rate, galvanic skin response, or a profile of mood states (POMS). Two of the studies included no measures of mood or arousal [30, 32]. A summary of the measures and results is provided in Table 2.

Studies with a unilateral neglect group reported variable effects of music on mood outcomes. One of the studies found no effect on mood with researcher selected music [33]. Another study [29] found improvements in mood and arousal with self-selected pleasant music and decreases with self-selected unpleasant music and white noise. Only one of the parallel group RCTs included a mood outcome measure [31]. They observed no significant interaction between group and time but the music listening group was found to have significantly lower levels of depression compared to treatment as usual at 3 months, and a marginal difference in their confusion score. Marginal differences in depression and confusion were also found at 6 months compared to usual care.

### 3.4.2 Cognition

Unilateral neglect was assessed using three different subtests: the Star Cancellation Test (SCT), Line Bisection Test (LBT) and the Picture Scanning Test (PST) of the Behavioural Inattention Test (BIT) or picture copying. Other measures of cognition included a brief

cognitive screen (MMSE) and a detailed cognitive assessment battery covering 10 different cognitive domains. A summary of the measures and results is provided in Table 2.

The effects of cognition were variable in the neglect group. One of the studies found listening to classical music and non-verbal auditory stimuli to reduce left-side neglect [30]. Improvement in SCT performance was reported with self-selected pleasant music [29] but not in a study using researcher selected music [33]. Improvement in PST performance was reported for listening to pleasant music [29]. Another study also reported improvements in PST performance with classical music compared to white noise or silence [33]. Performance with white noise was also significantly better compared to silence [33]. Neither study found significant change in LBT performance.

Both parallel group RCTs reported improvements in cognitive performance following music listening. The music group was found to show greater improvements on MMSE performance compared to control [32]. This finding was not reported separately for those with stroke and head injury. The other study [31] reported significant improvement in focussed attention for music listening at 3 months and 6 months post-stroke. Focused attention in the music listening group was also marginally better compared to audiobook listening at 3 months and significantly better at 6-months post-stroke. Significant improvements were also reported in verbal memory at 3 months compared to audiobook listening and usual care and at 6 months compared to audiobook listening.

### **3.5 Risk of bias**

Quality of the included studies was variable (Table 3 and Figure 2). Most studies, with the exception of one [31], reported insufficient detail to allow accurate assessment of all the

important domains of our quality assessment tools. With music listening interventions it is difficult to conceal the intervention from the participant (the listener) thus participant blinding was not used in any of the studies included. None of the studies reported any adverse outcomes.

### ***3.6 Ongoing or unpublished controlled trials***

In addition to the five studies included in the review, four studies of music listening not yet published were identified. Recruitment or analyses are ongoing and as these studies are not yet published in peer reviewed scientific journals we did not include them in our evidence synthesis. However, we offer brief synopsis and preliminary results where available.

Two of the studies are ongoing [34, 35] and two have recently completed [36, personal communication]. One study [34] assesses the effects of music listening on stress parameters by comparing instrumental music listening to music listening with lyrics and usual care. Outcomes are expected on cognition, mood and physiological stress parameters (cortisol, endorphin, oxytocin) at baseline, 3-months and 6-months post-stroke. The second study [35] assesses the effects of music listening, music listening with brief mindfulness training and audiobook listening on attention, memory and mood during the first 6 months post-stroke. In addition to cognitive and mood outcomes, the study is expected to report qualitative data about participants' experience of engaging in the interventions.

One of the recently completed studies [36] compared preferred music listening with usual care in an inpatient setting, describing outcomes of mood, cognition, functioning and quality of life. The study is yet to report definitive findings but preliminary data suggests no group differences in mood and cognition at 3-months post-stroke but suggest improvements in

quality of life and functioning at 6-months post-stroke in the music listening group. The other recently completed study compared Nordoff Robbins Music Therapy (NRMT) to preferred music listening and usual care delivered over 1-2 inpatient sessions and assessed by a blind assessor. Decreases in negative emotion were found following NRMT. No significant change in either positive or negative emotions were found in the preferred music listening group and a significant increase in positive emotion was found in the control group [personal communication].

#### **4. DISCUSSION**

Our review of the published literature suggests that music may have beneficial effects on post-stroke mood and cognition. It is encouraging that all studies reported benefits on at least one of the mood or cognitive domains tested as outcome measures.

This review benefits from a comprehensive search, spanning large numbers of databases, music therapy journals and conferences proceedings. We followed PRISMA guidance and embedded internal and external validation steps within our review. However, the data are far from definitive. Only one study was judged to be of high methodological quality with a low risk of bias [31]. Despite using a wide inclusion criterion to include all types of music listening based interventions, only five published studies were identified, each with modest sample size. In this situation, meta-analysis can have utility but the heterogeneity across studies precluded any attempt at meaningful summary analysis. We note the inconsistency in outcome assessments employed to describe mood and cognition, this has been described in many other areas of stroke research [38]. Even if we had been able to pool data, the total number of participants across all the available studies was less than would be seen in a typical phase III study of a pharmacological intervention in stroke or dementia. It seems

implausible that music listening will have an effect size that is an order of magnitude greater than drug therapy and so we must conclude that larger studies and/or better ways of pooling data from existing trials are needed.

Focussing on the two studies with larger sample size, both assessed the cognitive effects of music listening beyond a brief exposure. One reported global improvements in cognition compared to usual care with no specific control intervention [32]. However, this finding was not reported separately for those with stroke and head injury and thus should be interpreted with care. The second study [31] reported improvements in verbal memory and focused attention domains following music listening compared to an active control intervention, and usual care. Improvements on tasks of visual attention in the included studies with individuals experiencing unilateral neglect also suggests that attentional processes may partly mediate the positive effects of music listening. Studies utilising brain imaging technology have also reported that music listening engages neural networks involved in attention [37].

The generalisability of the findings of this review may be limited given the heterogeneity of the sample. Due to the small number of studies identified it was not possible to examine the effects of music listening in the early (acute) versus later (chronic) stages of recovery, between in and outpatient settings or between those with the first or subsequent stroke. Future work should explore these areas in more detail. The quality of reporting was marginal with only three studies detailing the method of randomisation used. Similarly, only two of the studies utilised blind outcome assessments. The main driver for the risk of bias was intervention allocation with only one study reporting allocation concealment.

Accepting the limitations of the evidence, the included studies challenge some of the accepted theories regarding music as a therapeutic intervention. For example, participant selected music seemed to be just as efficacious as interventions delivered by a specialist music therapist and music exposure of minutes delivered over a few sessions seemed to have benefit, suggesting prolonged music listening may not be required.

The included studies also highlight areas that need more attention paid in future studies of music listening. The outcomes tended to be focussed on the period immediately following delivery of the intervention. Maintenance of effect and improved everyday functioning will be important for a chronic condition such as stroke and future studies should have longer follow up. The mechanism of the domain specific effects should be explored further. An impairment focus in the included outcomes does not allow us to say anything about how improvements in cognition and mood translate to those outcomes that are important to patients, namely improved function, societal participation or quality of life [39]. We should not assume that a modest domain specific improvement is associated with meaningful gains on other broader measures of recovery and studies of music listening in other conditions supports this stance [40].

Currently, there is insufficient evidence to recommend the use of music listening in routine clinical care post-stroke. Overall, music listening based interventions show promise in improving mood and alleviating cognitive deficits post-stroke but available data are not yet sufficient to change guidelines or policy. We need studies with larger samples and better methodological quality to understand the effect of music listening; how music listening based interventions are best delivered, and who can benefit from them. We await the

results of ongoing studies and would hope that with an increasing evidence base quantitative synthesis of pooled data may be possible.



## **5. Expert commentary**

Issues with low mood, attention and memory are common following stroke but the evidence base for therapeutic interventions is sparse. Music has the ability to evoke positive emotion and relaxation and may offer an avenue for developing interventions without the side effects associated with pharmacological therapies or the substantial cognitive demands required for traditional psychological therapies. Available evidence is not sufficiently robust to make recommendations about using music listening in post-stroke rehabilitation. However, there is a strong signal of potential benefit from music listening and the findings of our review are encouraging for guiding further research. It is encouraging that larger, high quality studies of music listening interventions are currently ongoing and we await these results eagerly. Future work should focus on understanding the effects and mechanism of action of music listening based interventions at different stages of stroke recovery and should describe the implementation of music listening into stroke practice.

## **6. Five year review**

There is a gradual increase in the recognition of the importance mood and cognition play in recovery following a stroke. Use of music listening in medical care is an emerging field and has the potential to offer low cost, non-invasive, safe and less resource demanding interventions compared to traditional music and psychological therapies. The available data are encouraging but future research needs to focus on understanding the key ingredients of these interventions and how they may moderate changes in attention, memory, mood and arousal at different stages of the recovery process and which individuals are likely to benefit most from these interventions. Our searches identified four ongoing or recently completed studies involving music listening post-stroke from Australia, Finland and two from the UK with no published data, hence the next five years should see a marked increase in the number of RCT reporting mood and cognitive outcomes following music listening interventions post-stroke. This should allow the effects of these interventions to be studied in greater detail and to work towards developing treatment recommendations for clinical care. It is particularly important to develop a better understanding of the long term effects of regular music listening based interventions beyond single testing sessions given that studies investigating the effect of music listening on reducing neglect tend to utilise a single session method. There is also need to improve the methodological quality of studies with larger sample sizes and studies that include active control groups, functional outcomes and the impact of these interventions on quality of life. Should music listening based interventions continue to show promise in improving outcomes, this would have the potential to better utilise sedentary time spent at a stroke ward or at home while enhancing cognitive recovery and psychological wellbeing after stroke.

## 7. Key issues:

- Emotional problems such as depression and cognitive deficits, particularly in the attention, memory and executive function domains, are common after stroke.
- The evidence base for improving emotional and cognitive issues and attention post-stroke is limited.
- Music listening is a non-invasive, low cost intervention compared to many standard psychological treatment interventions.
- There is limited published evidence on music listening for improving psychological wellbeing post-stroke although all available studies suggest beneficial effects of the intervention.
- Available studies suffer from small sample size, poor reporting and potential biases and no firm recommendations on the use of music listening in stroke can be made.
- Sufficiently powered studies with improved methodological quality are needed before use of music listening based interventions can be recommended to be used in clinical practice.
- A number of studies describing psychological effects of music listening post stroke are ongoing and their results may resolve some of the uncertainty.

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**Conflicts of interest**

None

## References

\* of interest

\*\* of considerable interest

1. Adamson J, Beswick A, Abraham S. Is stroke the most common cause of disability? *Journal of Stroke and Cerebrovascular Diseases*; 2004;13, 4, 171-177.
2. Mozaffarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics – 2015 Update: a report from the American Heart Association. *Circulation*. 2015;131:e29-e322.
3. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson L, Truelsen T, O'Donnell M, Venketasubramanian N, Barker-Collo, S, Lawes CMM, Wang W, Shinohara Y, Witt E, Ezzati M, Naghavi M, Murray C. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. *The Lancet*; 2014: 383, 9913, 245-255. DOI: 10.1016/S0140-6736(13)61953-4
4. De Wit L, Putman K, Baert I, Lincoln N, Angst F, Beyens H, Bogaerts K, Brinkmann N, Connell L, Dejaeger E, De Weerdts W, Jenni W, Kaske C, Komarek A, Lesaffre E, Leys M, Louckx F, Schuback B, Schupp W, Smith B, Feys H. Anxiety and depression in the first six months after stroke. A longitudinal multicentre study, *Disability and Rehabilitation*; 2008: 30, 24: 1858 – 1866. doi: 10.1080/09638280701708736
5. Lincoln NB, Brinkmann N, Cunningham S, Dejaeger E, De Weerdts W, Jenn, W, Mahdzir A, Putman K, Schupp W, Schuback B, De Wit L. Anxiety and depression after stroke: a 5 year follow-up. *Disability and Rehabilitation*; 2013;35, 2: 140-145. doi: 10.3109/09638288.2012.691939.

6. Hurford R, Charidimou A, Fox Z, Cipolotti L, Werring D.J. Domain-specific trends in cognitive impairment after acute ischaemic stroke. *Journal of Neurology*; 2013;260: 237-241. doi: 10.1007/s00415-012-6625-0.
7. Bour A, Rasquin S, Aben I, Boreas A, Limburg M, Verhey F. A one-year follow-up study into the course of depression after stroke. *J Nutr Health Aging*; 2010;14:488-493.
8. Cumming TB, Marshall RS, Lazar RM. Stroke, cognitive deficits, and rehabilitation: still an incomplete picture. *International Journal of Stroke*; 2013; 8: 38–45. doi: 10.1111/j.1747-4949.2012.00972.x
9. Jaracz, K, Jaracz J, Kozubski W, Rybakowski J.K. Post-stroke quality of life and depression. *Acta Neuropsychiatrica*; 2002;14: 219–225. doi: 10.1034/j.1601-5215.2002.140504.
10. Pollock A, St George B, Fenton M, Firkins L. Top 10 research priorities relating to life after stroke – consensus from stroke survivors, caregivers, and health professionals. *Int J Stroke*; 2012; 9, 313-320. doi: 10.1111/j.1747-4949.2012.00942.x.
11. McArthur KS, Quinn TJ, Higgins P, Langhorne P. Post-acute care and secondary prevention after ischaemic stroke. *BMJ* 2011; 342:d2083
12. Hackett ML, Anderson CS, House A, Xia J. Interventions for treating depression after stroke. *Cochrane Database of Systematic Reviews*; 2008: 4:Art.No.CD003437. doi: 10.1002/14651858.CD003437.pub3
13. Broomfield, N. M., Laidlaw, K., Hickabottom, E., Murray, M. F., Pendrey, R., Whittick, J. E. and Gillespie, D. C. Post-stroke depression: the case for augmented, individually tailored cognitive behavioural therapy. *Clin. Psychol. Psychother*; 2011; 18: 202–217. doi: 10.1002/cpp.711
14. Sue D, Sue D.E, Sue S. *Understanding abnormal behaviour*, 2010. Boston, MA: Wadsworth.

15. Aldridge D. An overview of music therapy research, *Complementary Therapies in Medicine*; 1994:2,4, 204-216.
16. \*\* Särkämö T, Soto D. Music listening after stroke: Beneficial effects and potential neural mechanisms. *Annals of the New York Academy of Sciences*; 2012: 1252, 266-281. doi:10.1111/j.1749-6632.2011.06405.x A generic review of the effects of music listening after stroke.
17. Brown, S., M.J. Martinez, and L.M. Parsons, Passive music listening spontaneously engages limbic and paralimbic systems. *Neuroreport*; 2004: 15, 13, 2033-7.
18. Schlaug, G., E. Altenmüller, and M. Thaut, Music Listening and Music Making in the Treatment of Neurological Disorders and Impairments. *Music Perception: An Interdisciplinary Journal*; 2010: 27, 4, 249-250.
19. Chanda, M.L. and D.J. Levitin, The neurochemistry of music. *Trends Cogn Sci*; 2013: 17, 4, 179-93.
20. Mavridis, I.N., Music and the nucleus accumbens. *Surg Radiol Anat*; 2015: 37, 2, 121-5.
21. Raglio, A., et al., Effects of music and music therapy on mood in neurological patients. *World J Psychiatry*; 2015: 5, 1, 68-78.
22. Soto, D., et al., Pleasant music overcomes the loss of awareness in patients with visual neglect. *Proc Natl Acad Sci U S A*; 2009: 106, 4, 6011-6.
23. Wilkins, R.W., et al., Network science and the effects of music preference on functional brain connectivity: from Beethoven to Eminem. *Sci Rep*; 2014: 4, 6130.
24. \*Särkämö T, Ripollés P, Vepsäläinen H, Autti T, Silvennoinen HM, Salli E, Laitinen S, Forsblom A, Soynila S and Rodríguez-Fornells A. Structural changes induced by daily

music listening in the recovering brain after middle cerebral artery stroke: a voxel-based morphometry study. *Front. Hum. Neurosci*; 2014: 8,245. doi: 10.3389/fnhum.2014.00245. Paper reporting grey matter changes in the brain relating to reference 30 (Särkämö et al.) following music listening post-stroke.

25. Chan MF, Wong ZY, Thayala NV. The effectiveness of music listening in reducing depressive symptoms in adults: a systematic review. *Complement Ther Med*; 2011;19,6,:332-48. doi: 10.1016/j.ctim.2011.08.003.
26. Hole J, Hirsch M, Ball E, Meads C. Music as an aid for postoperative recovery in adults: A systematic review and meta-analysis. *The Lancet*; 2015: 386 , 10004, 1659-1671. Doi: 10.1016/S0140-6736(15)60169-6.
27. Ueda T, Suzukamo Y, Sato M, Izumi S-I. Effects of music therapy on behavioral and psychological symptoms of dementia: A systematic review and meta-analysis. *Ageing Research Reviews*; 2013;12, 2: 628-641.
28. \*\* Bradt J, Magee WL, Dileo C, Wheeler BL, McGilloway E. Music therapy for acquired brain injury. *Cochrane Database of Systematic Reviews*; 2010: 7: CD006787. DOI: 10.1002/14651858.CD006787.pub2. Systematic review reporting potential beneficial effects of music therapy on gait parameters in acquired brain injury.
29. \* Chen MC, Tsai P-L, Huang Y-T, Lin K-C. "Pleasant music improves visual attention in patients with unilateral neglect after stroke." *Brain Injury*; 2013: 27, 1: 75-82. 10.3109/02699052.2012.722255. A study investigating the effects of participant selected pleasant music and unpleasant music on mood and unilateral neglect post-stroke. Study included in the systematic review.
30. \*Hommel M, Peres, B, Pollak P, Memin B, Besson G, Gaio J-M, Perret J. Effects of Passive Tactile and Auditory Stimuli on Left Visual Neglect. *Arch Neurol*. 1990;47,5:573-576.



31. \*\* Särkämö T, Tervaniemi M, Laitinen S, Forsblom A, Soinila S, Mikkonen M, Autti T, Silvennoinen HM, Erkkilä J, Laine M, Peretz I, Hietanen M.. "Music listening enhances cognitive recovery and mood after middle cerebral artery stroke." *Brain*; 2008; 131: 866-876. doi:10.1093/brain/awn013. Study examining the effects of music listening on mood and cognition during the first 6-months after stroke. Study included in the systematic review.
32. \* Singh SB, Chakraborty S, Jha KM, Haider S, Chandra S. "Repeated measure analysis in raga therapy: A case study on head injury patients." *Research Journal of Pharmaceutical, Biological and Chemical Science*; 2013; 4,1: 420-428. Study reporting the effects of raga listening following stroke and head injury. Study included in the systematic review.
33. \*Tsai P-L, Chen M-C, Huang Y-T, Lin K-C, Chen K-L, Hsu Y-W. "Listening to Classical Music Ameliorates Unilateral Neglect After Stroke." *American Journal of Occupational Therapy*; 2013;67,3: 328-335. doi: 10.5014/ajot.2013.006312. A study comparing classical music listening with white noise and silence. Study included in the systematic review.
34. Soinila S. et al., Music Listening and Stroke Recovery (MUKU2). <https://clinicaltrials.gov/ct2/show/NCT01749709?term=NCT01749709&rank=1>  
[Last accessed 2 April 2016]
35. Evans J, Baylan S. et al., Listening for Leisure after Stroke (MELLO). <https://clinicaltrials.gov/ct2/show/NCT02259062?term=mello&rank=1>  
[Last accessed 2 April 2016]
36. Hewitt L, Sanctuary C. Stroke sounds: Music listening in stroke rehabilitation. *Int J Stroke*; 2015; 10, 3 suppl, 64. doi: 10.1111/ijss.12585.

37. Sridharan D.J, Levitin C.H, Chafe J, Berger V. Menon. Neural dynamics of event segmentation in music: Converging evidence for dissociable ventral and dorsal networks. *Neuron*; 2007, 55, 521–532. doi:10.1016/j.neuron.2007.07.003/.
38. Lees R, Fearon P, Harrison Jk, Broomfield NM, Quinn TJ. Cognitive and mood assessment in stroke research focused review of contemporary studies. *Stroke*; 2012; 43:1678-80.
39. Quinn TJ, McArthur K, Ellis G, Stott DJ. Functional assessment in older people. *BMJ*; 2011; 343:d4681.
40. Archie P, Bruera E, Cohen L. Music-based interventions in palliative cancer care: a review of quantitative studies and neurobiological literature. *Support. Care Cancer*; 2013; 21, 2609–2624 10.1007/s00520-013-1841-4

**Table 1: Characteristics of included studies**

| <b>Study, Year, Country</b> | <b>Type of Intervention</b>  | <b>Music selection</b>                           | <b>Dose, design</b>                                       | <b>N, (per group)</b> | <b>Stroke type, % ischaemic</b>                            | <b>Time since stroke (Mean)</b> | <b>Mean Age (years)</b> |
|-----------------------------|--|--|---|-----------------------|--|---------------------------------|-------------------------|
| Chen et al., 2013, Taiwan   | Pleasant music (3 pieces) and unpleasant music (3 pieces) listening. White noise used as a control condition.                                | Participant selected                             | 1 session of each condition within 1 week, within-subject | 19                    | Unilateral neglect following right hemisphere stroke, 100% | 15mths                          | 66.1                    |
| Hommel et al., 1990, France | 1) no stimulation<br>2) no stimulation<br>3) tac. stim. R cheek<br>4) tac. stim. L cheek<br>5) tac. stim. both cheeks<br>6) headphones alone | Researcher selected (Bach and Vivaldi concertos) | Single session, within-subject                            | 14                    | Unilateral neglect following right hemisphere stroke, 86%  | 15 days                         | 57.0                    |

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- 7) verbal stimulation  
(landscape)
- 8) verbal stimulation  
(encouragement)
- 9) classical music
- 10) white noise

|                                  |  |                         |  |                       |  |          |      |
|----------------------------------|--|-------------------------|--|-----------------------|--|----------|------|
| Särkämö et al.,<br>2008, Finland | Music listening or<br>audiobook or TAU   | Participant<br>selected | 1hr daily<br>for 8 wks,<br>single-<br>blind RCT                      | 60<br>(19, 19,<br>17) | Fist MCA,<br>100%  | 8.7 days | 58.8 |
| Singh et al., 2013,<br>India     | 10 different<br>Hindustani ragas<br>listened at specific<br>times during the day<br>or TAU | Researcher<br>selected  | 10 x<br>20mins<br>(=3hrs<br>20mins)<br>daily for<br>six mths,<br>RCT | 60<br>(30, 30)        | NSt, NSt but<br>sample<br>includes<br>diffuse head<br>injury | NSt      | 55.5 |

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|                             |  |  |   |    |   |             |      |   |
|-----------------------------|--|--|---|----|---|-------------|------|---|
| Tsai et al. 2013,<br>Taiwan | Classical music,<br>white noise, silence | Researcher<br>selected (Mozart's<br>Sonata for two<br>pianos in D major,<br>K. 448 and Vivaldi's<br>Spring from the<br>Four Seasons) | 3 Single<br>sessions<br>within one<br>week,<br>within-<br>subject | 16 | Unilateral<br>neglect<br>following right<br>hemisphere<br>stroke, NSt | 13.8 months | 64.4 | , |
|-----------------------------|--|--|---|----|---|-------------|------|---|

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MCA= Middle Cerebral Artery stroke, NSt = Not stated, RCT = randomised controlled trial, Tac Stim = Tactile stimulation, TAU = treatment as usual

**Table 2. Outcome assessments and results of included studies**

| Study                | Outcome Assessments |   | Results  |  |
|----------------------|---------------------|---|--|--|
|                      | Mood & Arousal      | Cognition & QoL                                       | Mood & Arousal   | Cognition & Quality of Life  |
| Chen et al., 2013    | VAS, HR, GSR        | SCT, LBT, PST,<br>Visual Exploration Task             | Increase in positive emotion on VAS [p<.05] and arousal [p<.001] for pleasant music, decreases for unpleasant music and white noise. HR (p=0.29) and GSR (p = .26) ns. | Improvement in SCT [p=0.01] and PST for pleasant music [p<0.1]; ns. change in LBT [p=.59]; Improved performance on VET with pleasant music [p=.01]. Unpleasant music > white noise ns. |
| Hommel et al., 1990  | n/a                 | six drawing copying tests                             | n/a  | Reduction in unilateral neglect with music and non-verbal auditory stimulation [p <.01], and white noise [p < .01] only.   |
| Särkämö et al., 2008 | POMS                | Cognitive test battery assessing 10 cognitive domains | Significantly lower depression for music listening compared to TAU [p<.05] at 3 months, marginal   | Significant improvement in FA for music listening at 3 months compared to TAU [p<.05], marginally to AB [p=.058] and at 6-   |

|                    |     |               |  |   |
|--------------------|-----|---------------|--|---|
|                    |     | SAQOL-39      | <p>difference in confusion [p=.06], at 6 months marginal difference in depression [p= .07] and confusion [p=.06] in the music group compared to TAU.</p> | <p>months compared to AB [p&lt;.05] and TAU [p&lt;.01]; significant improvement in VM at 3 months compared to AB [p&lt;.001] and TAU [p&lt;.05] and at 6 months compared to AB [p&lt;.01], no differences in self or other rated QoL at 3 or 6 months [p= .094-.987].</p> |
| Singh et al., 2013 | n/a | MMSE          | n/a  | <p>No differences in MMSE score at baseline. significant difference between intervention and control group at discharge, one, three and six month follow-up (p&lt;.01)</p>  |
| Tsai et al. 2013   | VAS | SCT, LBT, PST | VAS ns.  | <p>SCT and LBT performance ns. PST improved performance with classical music &gt; white noise [p&lt;.05] and classical music &gt; silence [p&lt;.01]. White noise &gt;silence</p>   |

[p<.05].

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AB=audiobooks, FA = Focused Attention, GSR = Galvanic Skin Response, HR = Heart rate, ns. = non significant, LBT = Line Bisection Test, MMSE, Mini Mental State Examination, POMS = Profile of Mood States, PST = Picture Scanning Test, QoL = Quality of Life, SAQOL-39 = Stroke and Aphasia Quality of Life Scale-39, SCT = Star Cancellation Test, TAU = treatment as usual, VAS = Visual Analogue Scale, VET=Visual Exploration Task, VM = Verbal Memory

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**Table 3: Quality of included studies**

| <b>Study<br/>(author, year)</b> | <b>Random<br/>sequence<br/>generation</b> | <b>Allocation<br/>concealment</b> | <b>Blinding of<br/>participants<br/>and personnel</b> | <b>Blinding of<br/>outcome<br/>assessment</b> | <b>Incomplete<br/>outcome<br/>data</b> | <b>Selective<br/>outcome<br/>reporting</b> |
|---------------------------------|---|-----------------------------------|---|---|--|--|
| Chen (2013)                     | Low                                       | Unclear                           | High  | Unclear                                       | Low                                    | Low  |
| Hommel (1990)                   | Unclear                                   | Unclear                           | High  | Low   | Unclear                                | Low  |
| Särkämö (2008)                  | Low                                       | Low                               | High  | Low   | Low                                    | Low  |
| Singh (2013)                    | High                                      | High                              | High  | Unclear                                       | Low                                    | Low  |
| Tsai (2013)                     | Low                                       | Unclear                           | High  | Unclear                                       | Low                                    | Low  |